REMARKS

By the present Amendment, Claim 274 has been added, which is essentially identical to Claim 6 (including the limitations of Claim 1 from which it depends) of U.S. Patent No. 6,605,449, issued to Short ("the '449 patent). Claim 275 has also been added, which contains language substantially similar to Claim 274.

Support for Claims 274 and 275 can be found in the Appendix hereto. Claim 6 of the '449 patent has been copied to avoid any question of compliance with 35 U.S.C. §135(b). After completing their assessment of the issues, a decision will be made by Applicants regarding filing a Request for Interference with the '449 patent. If the Examiner should need to act on the application prior to that time, he or she is invited to contact the undersign using the information below.

Respectfully submitted,

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APPENDIX

Claim	Exemplary Support in U.S.S.N. 10/646,221
A method of producing a progeny library	p. 2, l. 24 – p. 3, l. 5, Claim 16 ("a method...to generate a library..."); p. 16, ll. 18-20 ("starting DNA segments are recombined...to generate a diverse library of recombinant DNA segments")
comprised of chimerized	p. 31, ll. 32-35 ("nucleic acids encoding protein modules can be exchanged...to generate novel and functional chimeric polyketides"); p. 37, ll. 20-21 ("A library of 10^4 chimeric interferon genes...");
but pre-determined polynucleotide sequences	Claim 16 ("a first and second substrate molecules ...comprise defined segments")
each of which is comprised of a pre-determined number of building block sequences	Claim 16 ("a first and second substrate molecules ...comprise defined segments"); p. 32, l. 6 – p. 34, l. 9 (e.g., "assemble multiple segments"); Example III, p. 89, l. 36 – p. 93, l. 9 (e.g., "The modeled structure...has been divided into nine segments based on a combination of criteria of maintaining secondary structure elements as single units and placing/choosing placement of the segment boundaries in regions of high identity.")
that are assembled in non-random order,	p. 33, l. 12 ("are reassembled in an ordered fashion...")
the method comprising:	p. 2, l. 29 ("the method comprising...")
generating a plurality of pre-determined nucleic acid building block sequences obtained from polynucleotide sequences	p. 29, ll. 22-27 ("The coarse grain methods allow one to exchange chunks of genetic material between substrate nucleic acids thereby limiting diversity in the resulting recombinants to exchanges or substitutions of domains, restriction fragments, oligo-encoded blocks of mutations, or other arbitrarily defined segments..."); p. 32, ll. 9-11 ("multiple segments that have been separately evolved..."); p. 32, ll. 17-20 ("Boundaries defining segments of a nucleic acid sequence of interest...")
encode enzymes or fragments thereof	p. 43, ll. 18-20 ("this technique can be used to evolve bovine intestinal alkaline phosphatase (BIAP)..."; p. 82, ll. 16-25 ("Evolution of BIAP...the oligonucleotides are assembled into full-length genes as described above."); p. 16, ll. 22-26 ("In general, the starting segments and the recombinant libraries generated include full-length coding sequences...However, if this is not the case...")
and comprised of sequences delineated by demarcation points	p. 32, ll. 17-20 ("Boundaries defining segments of a nucleic acid sequence of interest preferably lie

selected from aligned progenitor sequences; and	in intergenic regions, introns, or areas of a gene not likely to have mutations of interest; p. 38, ll. 23-28 ("This region, which can be part or all of a gene or a gene is arbitrarily delineated into segments. The segment borders can be chosen randomly, based on correspondence with natural exons, based on structural considerations (loops, alpha helices, subdomains, whole domains, hydrophobic core, surface, dynamic simulations), and based on correlations with genetic mapping data.)
non-stochastically reassembling said nucleic acid building block sequences	p. 33, l. 12 ("reassembled in an ordered fashion")
to produce said chimerized but pre-determined polynucleotide sequences,	p. 31, ll. 32-35 ("nucleic acids encoding protein modules can be exchanged...to generate novel and functional chimeric polyketides"); p. 37, ll. 20-21 ("A library of 10^4 chimeric interferon genes..."); Claim 16 ("a first and second substrate molecules ...comprise defined segments")
such that a designed overall assembly order is achieved	p. 33, l. 12 ("reassembled in an ordered fashion")
for each of said chimerized but pre-determined polynucleotide sequence.	p. 31, ll. 32-35 ("nucleic acids encoding protein modules can be exchanged...to generate novel and functional chimeric polyketides"); p. 37, ll. 20-21 ("A library of 10^4 chimeric interferon genes..."); Claim 16 ("a first and second substrate molecules ...comprise defined segments")
275. A method of producing a library	p. 2, l. 24 – p. 3, l. 5, Claim 16 ("a method...to generate a library..."); p. 16, ll. 18-20 ("starting DNA segments are recombined...to generate a diverse library of recombinant DNA segments")
comprised of chimerized	p. 31, ll. 32-35 ("nucleic acids encoding protein modules can be exchanged...to generate novel and functional chimeric polyketides"); p. 37, ll. 20-21 ("A library of 10^4 chimeric interferon genes...");
but defined polynucleotide sequences	Claim 16 ("a first and second substrate molecules ...comprise defined segments")
each of which is comprised of a defined number of polynucleotide segments	Claim 16 ("a first and second substrate molecules ...comprise defined segments"); p. 32, l. 6 – p. 34, l. 9 (e.g., "assemble multiple segments"); Example III, p. 89, l. 36 – p. 93, l. 9 (e.g., "The modeled structure...has been divided into nine segments based on a combination of criteria of

	maintaining secondary structure elements as single units and placing/choosing placement of the segment boundaries in regions of high identity.")
that are assembled in an ordered fashion,	p. 33, l. 12 ("are reassembled in an ordered fashion...")
the method comprising:	p. 2, l. 29 ("the method comprising...")
a) generating a plurality of defined polynucleotide segments of substrate nucleic acid sequences	p. 29, ll. 22-27 ("The coarse grain methods allow one to exchange chunks of genetic material between substrate nucleic acids thereby limiting diversity in the resulting recombinants to exchanges or substitutions of domains, restriction fragments, oligo-encoded blocks of mutations, or other arbitrarily defined segments..."); p. 32, ll. 9-11 ("multiple segments that have been separately evolved..."); p. 32, ll. 17-20 ("Boundaries defining segments of a nucleic acid sequence of interest...")
that encode full-length enzymes,	p. 43, ll. 18-20 ("this technique can be used to evolve bovine intestinal alkaline phosphatase (BIAP)..."; p. 82, ll. 16-25 ("Evolution of BIAP...the oligonucleotides are assembled into full-length genes as described above."); p. 16, ll. 22-24 ("In general, the starting segments and the recombinant libraries generated include full-length coding sequences...")
and wherein the borders defining the polynucleotide segments are selected from the aligned substrate nucleic acid sequences; and	p. 32, ll. 17-20 ("Boundaries defining segments of a nucleic acid sequence of interest preferably lie in intergenic regions, introns, or areas of a gene not likely to have mutations of interest; p. 38, ll. 23-28 ("This region, which can be part or all of a gene or a gene is arbitrarily delineated into segments. The segment borders can be chosen randomly, based on correspondence with natural exons, based on structural considerations (loops, alpha helices, subdomains, whole domains, hydrophobic core, surface, dynamic simulations), and based on correlations with genetic mapping data.)
reassembling said defined polynucleotide segments in order	p. 33, l. 12 ("reassembled in an ordered fashion")
thereby producing the library of chimerized but defined polynucleotide sequences,	p. 31, ll. 32-35 ("nucleic acids encoding protein modules can be exchanged...to generate novel and functional chimeric polyketides"); p. 37, ll. 20-21 ("A library of 10^4 chimeric interferon genes..."); Claim 16 ("a first and second substrate molecules ...comprise defined

	segments")
such that said segments are reassembled in an ordered fashion	p. 33, l. 12 ("reassembled in an ordered fashion")
for each chimerized but defined polynucleotide sequences encoding full-length enzymes.	p. 31, ll. 32-35 ("nucleic acids encoding protein modules can be exchanged…to generate novel and functional chimeric polyketides"); p. 37, ll. 20-21 ("A library of 10^4 chimeric interferon genes…"); Claim 16 ("a first and second substrate molecules …comprise defined segments")